



ATTORNEYS AT LAW



Robert Greene Sterne
 Edward J. Kessler
 Jorge A. Goldstein
 David K.S. Cornwell
 Robert W. Esmond
 Tracy-Gene G. Durkin
 Michele A. Cimbala
 Michael B. Ray
 Robert E. Sokohl
 Eric K. Steffe
 Michael Q. Lee
 Steven R. Ludwig
 John M. Covert
 Linda E. Alcom
 Robert C. Millonig
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 Donald J. Featherstone
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 Brian J. Del Buono
 Virgil Lee Beaston
 Kimberly N. Reddick

Theodore A. Wood
 Elizabeth J. Haanes
 Joseph S. Ostroff
 Frank R. Cottingham
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 Jason D. Eisenberg
 Michael D. Specht
 Andrea J. Kamage
 Tracy L. Muller
 LuAnne M. Yuricek*
 John J. Figueira
 Ann E. Summerfield
 Tiera S. Coston*

Aric W. Ledford*
 Registered Patent Agents*
 Karen R. Markowitz
 Nancy J. Leith
 Helene C. Carlson
 Gaby L. Longsworth
 Matthew J. Dowd
 Aaron L. Schwartz
 Mary B. Tung
 Katrina Y. Pei Quach
 Bryan L. Skelton
 Robert A. Schwartzman
 Timothy A. Doyle
 Jennifer R. Mahalingappa
 Teresa A. Colella
 Jeffrey S. Lundgren

Victoria S. Rutherford
 Eric D. Hayes

Of Counsel
 Kenneth C. Bass III
 Evan R. Smith

*Admitted only in Maryland
 +Admitted only in Virginia
 •Practice Limited to
 Federal Agencies

January 20, 2004

WRITER'S DIRECT NUMBER:
 (202) 772-8637
INTERNET ADDRESS
 KAREN.M@SKGF.COM

Commissioner for Patents
 P.O. Box 1450
 Alexandria, VA 22313-1450

Re: U.S. Utility Patent Application
 Appl. No. 10/623,813; Filed: July 22, 2003
(Continuation-in-part of U.S. Appl. No. 09/720,086; § 102(e) date: July 23, 2001)
 For: ***De novo DNA Cytosine Methyltransferase***
Genes, Polypeptides and Uses Thereof
 Inventors: Li *et al.*
 Our Ref: 0609.4560003/JAG/KRM/DJN

Sir:

The following documents are forwarded herewith for appropriate action by the U.S. Patent and Trademark Office:

1. Information Disclosure Statement;
2. Form PTO-1449 (19 sheets citing documents AA1-AC1, AL1-AM1, and AR1-AT19);
3. A copy of document AT17; and
4. One (1) return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

Commissioner for Patents
January 20, 2004
Page 2

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

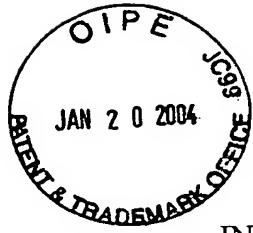
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Karen R. Markowicz
Agent for Applicants
Registration No. 36,351

KRM/DJN/cjs
Enclosures

SKOF_DC1:216129.1



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Li *et al.*

Appl. No. 10/623,813

Filed: July 22, 2003

For: ***De novo DNA Cytosine
Methyltransferase Genes,
Polypeptides and Uses Thereof***

Art Unit: *To Be Assigned*

Examiner: *To Be Assigned*

Atty. Docket:

0609.4560003/JAG/KRM/DJN

Information Disclosure Statement under 37 C.F.R. § 1.97(b)

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. A copy of document AT17 is provided.

A copy of documents **AA1** to **AC1** is not provided in accordance with the U.S. Patent and Trademark Office pre-OG notice of July 11, 2003, which states "[t]he Office hereby waives the requirement under 37 CFR 1.98 (a)(2)(i) for submitting a copy of each cited U.S. patent and each U.S. patent application publication for all U.S. national patent applications filed after June 30, 2003." Copies of all other documents were submitted to the Office in an IDS that complies with 37 C.F.R. § 1.98(a)-(c) in Application No. 09/720,086 (102(e) date: July 23, 2001), or cited by the Office during prosecution of said application which is relied upon for an earlier filing date under 35 U.S.C. § 120. Thus, copies of these documents are not attached. 37 C.F.R. § 1.98(d).

In accordance with 37 C.F.R. § 1.98(a)(3), Applicants' undersigned representative submits the following discussion of the relevance of the non-English language document **AM1** cited on Form PTO 1449:

Document **AM1** is in the Japanese language. An English language abstract of document **AM1** is attached as document **AT17**. In addition, an English language abstract can also be found on the front of **AM1**. Applicants note that document **AM1** was cited by the Examiner in parent application no. 09/720,086. In particular, in Paper No. 12, page 9, of the '086 application, the Examiner relied on accession no. AAT21884 on pages 991-992 of **AM1** and provided an alignment of accession no. AAT21884 and SEQ ID NOS:1 and 3 from the '086 application. The alignment is cited on the PTO-1449 as document **AR19**.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent

application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Karen R. Markowicz
Agent for Applicants
Registration No. 36,351

Date: January 20, 2004

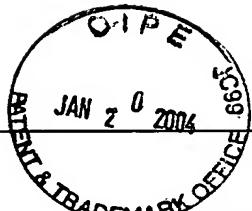
1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600



FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO. 0609.4560003/JAG/KRM/DJN	APPLICATION NO. 10/623,813
		APPLICANT Li <i>et al.</i>	
		FILING DATE July 22, 2003	GROUP <i>To Be Assigned</i>

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA1	5,578,716	11/26/1996	Szyf <i>et al.</i>			12/01/1993
	AB1	6,183,968 B1	02/06/2001	Bandman <i>et al.</i>			03/25/1999
	AC1	6,492,168 B1	12/10/2002	Kladde <i>et al.</i>			04/22/1999
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FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL1	WO 92/06985	04/30/1992	WIPO			Yes No
	AM1	WO 95/14772	06/01/1995	WIPO			Yes X No
	AN						Yes No
	AO						Yes No
	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	1	Aoki, A., <i>et al.</i> , "Enzymatic properties of <i>de novo</i> -type mouse DNA (cytosine-5) methyltransferases," <i>Nucl. Acids Res.</i> 29:3506-3512, Oxford University Press (September 2001)				
	AS	1	Ariel, M., <i>et al.</i> , "Gamete-specific methylation correlates with imprinting of the murine <i>Xist</i> gene," <i>Nat. Genet.</i> 9:312-315, Nature Publishing Group (1995)				
	AT	1	Ausubel, F.M., <i>et al.</i> , eds., "Expression of Proteins in Insect Cells Using Baculoviral Vectors," in <i>Current Protocols in Molecular Biology</i> , Greene Publishing Associates and Wiley-Interscience, New York, NY, pp. 16.8.1-16.11.7 (1990)				
EXAMINER		DATE CONSIDERED					

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.



FORM PTO-1449

INFORMATION DISCLOSURE STATEMENTATTY. DOCKET NO.
0609.4560003/JAG/KRM/DJNAPPLICATION NO.
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AM						Yes No
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AO						Yes No
AP						Yes No

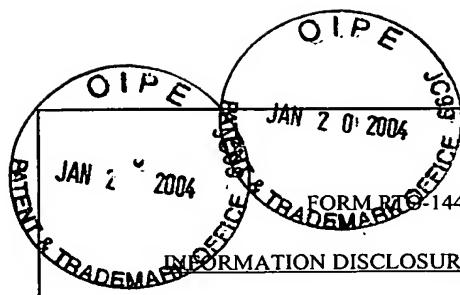
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	2	Bachman, K.E., <i>et al.</i> , "Dnmt3a and Dnmt3b Are Transcriptional Repressors That Exhibit Unique Localization Properties to Heterochromatin," <i>J. Biol. Chem.</i> 276:32282-32287, The American Society for Biochemistry and Molecular Biology, Inc. (August 2001)
AS	2	Baylin, S.B., <i>et al.</i> , "Alterations in DNA Methylation: A Fundamental Aspect of Neoplasia," <i>Adv. Cancer Res.</i> 72:141-196, Academic Press (February 1998)
AT	2	Bestor, T., <i>et al.</i> , "Cloning and Sequencing of a cDNA Encoding DNA Methyltransferase of Mouse Cells," <i>J. Mol. Biol.</i> 203:971-983, Academic Press (1988)

EXAMINER

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FOREIGN PATENT DOCUMENTS

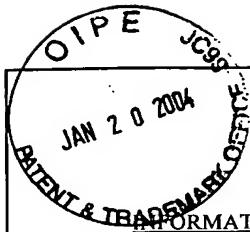
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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	3	Bestor, T.H., "Activation of mammalian DNA methyltransferase by cleavage of a Zn binding regulatory domain," <i>EMBO J.</i> 11:2611-2617, Oxford University Press (1992)
	AS	3	Brandeis, M., et al., "The ontogeny of allele-specific methylation associated with imprinted genes in the mouse," <i>EMBO J.</i> 12:3669-3677, Oxford University Press (1993)
	AT	3	Brockdorff, N., "Convergent themes in X chromosome inactivation and autosomal imprinting," in <i>Genomic Imprinting</i> , Reik, W., and Surani, A., eds., Oxford University Press, Oxford, UK, pp. 191-210 (December 1997)

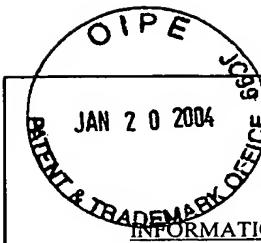
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FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>	ATTY. DOCKET NO. 0609.4560003/JAG/KRM/DJN	APPLICATION NO. 10/623,813
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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	4	Chaillet, J.R., <i>et al.</i> , "Parental-Specific Methylation of an Imprinted Transgene in Established during Gametogenesis and Progressively Changes during Embryogenesis," <i>Cell</i> 66:77-83, Cell Press (1991)				
	AS	4	Chen, T., <i>et al.</i> , "A Novel Dnmt3a Isoform Produced from an Alternative Promoter Localizes to Euchromatin and Its Expression Correlates with Active <i>de Novo</i> Methylation," <i>J. Biol. Chem.</i> 277:38746-38754, The American Society for Biochemistry and Molecular Biology, Inc. (October 2002)				
	AT	4	Cheng, X., "Structure and function of DNA methyltransferases," <i>Annu. Rev. Biophys. Biomol. Struct.</i> 24:293-318, Annual Reviews, Inc. (1995)				
EXAMINER		DATE CONSIDERED					
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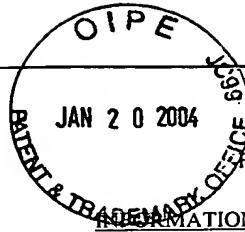
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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	5	Finnegan, E.J., and Dennis, E.S., "Isolation and identification by sequence homology of a putative cytosine methyltransferase from <i>Arabidopsis thaliana</i> ," <i>Nucl. Acids Res.</i> 21:2383-2388, Oxford University Press (1993)				
	AS	5	Flynn, J., <i>et al.</i> , "Murine DNA Cytosine-C ⁵ Methyltransferase: Pre-Steady- and Steady-State Kinetic Analysis with Regulatory DNA Sequences," <i>Biochem.</i> 35:7308-7315, American Chemical Society (1996)				
	AT	5	Flynn, J., <i>et al.</i> , "DNA Binding Discrimination of the Murine DNA Cytosine-C ⁵ Methyltransferase," <i>J. Mol. Biol.</i> 279:101-116, Academic Press (May 1998)				
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	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	6	Hata, K., <i>et al.</i> , "Dnmt3L cooperates with the Dnmt3 family of de novo DNA methyltransferases to establish maternal imprints in mice," <i>Develop.</i> 129:1983-1993, Company of Biologists Ltd. (April 2002)				
	AS	6	Jahner, D., and Jaenisch, R., "DNA Methylation in Early Mammalian Development," in <i>DNA Methylation. Biochemistry and Biological Significance</i> , Razin, A., eds., Springer-Verlag, New York, NY, pp. 189-219 (1984)				
	AT	6	Jentsch, S., <i>et al.</i> , "DNA methyltransferases affecting the sequence 5'CCGG," <i>Nucl. Acids Res.</i> 9:2753-2759, IRL Press (1981)				
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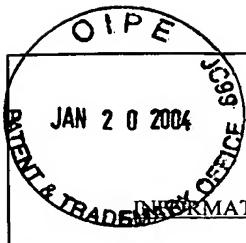
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	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	7	Jones, P.A., and Gonzalgo, M.L., "Altered DNA methylation and genome instability: A new pathway to cancer?," <i>Proc. Natl. Acad. Sci. USA</i> 94:2103-2105, National Academy of Sciences (March 1997)				
	AS	7	Klimašauskas, S., et al., "The sequence specificity domain of cytosine-C5 methylases," <i>Nucl. Acids Res.</i> 19:6183-6190, IRL Press at Oxford University Press (1991)				
	AT	7	Kumar, S., et al., "The DNA (cytosine-5) methyltransferases," <i>Nucl. Acids Res.</i> 22:1-10, Oxford University Press (1994)				
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O I P E
JAN 20 2004
U. S. PATENT & TRADEMARK OFFICE
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	8	Laird, P.W., and Jaenisch, R., "The Role of DNA Methylation in Cancer Genetics and Epigenetics," <i>Annu. Rev. Genet.</i> 30:441-464, Annual Reviews Inc. (1996)				
	AS	8	Lauster, R., et al., "Cytosine-specific Type II DNA Methyltransferases. A Conserved Enzyme Core with Variable Target-recognizing Domains," <i>J. Mol. Biol.</i> 206:305-312, Academic Press Ltd. (1989)				
	AT	8	Lazar, E., et al., "Transforming Growth Factor α : Mutation of Aspartic Acid 47 and Leucine 48 Results in Different Biological Activities," <i>Mol. Cell. Biol.</i> 8:1247-1252, American Society for Microbiology (1988)				
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	9	Lei, H., <i>et al.</i> , "De novo DNA cytosine methyltransferase activities in mouse embryonic stem cells," <i>Development</i> 122:3195-3205, The Company of Biologists Ltd. (1996)
	AS	2	Leonhardt, H., <i>et al.</i> , "A Targeting Sequence Directs DNA Methyltransferase to Sites of DNA Replication in Mammalian Nuclei," <i>Cell</i> 71:865-873, Cell Press (1992)
	AT	9	Li, E., <i>et al.</i> , "Targeted Mutation of the DNA Methyltransferase Gene Results in Embryonic Lethality," <i>Cell</i> 69:915-926, Cell Press (1992)

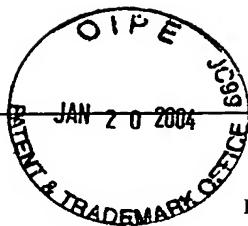
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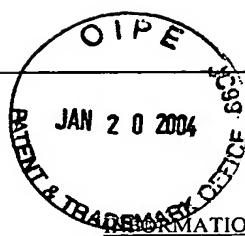
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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	<u>10</u>	Li, E., "Role of DNA methylation in mammalian development," in <i>Genomic Imprinting</i> , Reik, W., and Surani, A., eds., Oxford University Press, Oxford, UK, pp. 1-20 (December 1997)				
	AS	<u>10</u>	Malagnac, F., <i>et al.</i> , "A Gene Essential for De Novo Methylation and Development in Ascobolus Reveals a Novel Type of Eukaryotic DNA Methyltransferase Structure," <i>Cell</i> 91:281-290, Cell Press (October 1997)				
	AT	<u>10</u>	Narayan, A., <i>et al.</i> , "Hypomethylation of Pericentromeric DNA in Breast Adenocarcinomas," <i>Int. J. Cancer</i> 77:833-838, Wiley-Liss, Inc. (September 1998)				
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		APPLICANT Li et al.	
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	11	Okano, M., et al., "Dnmt2 is not required for <i>de novo</i> and maintenance methylation of viral DNA in embryonic stem cells," <i>Nucl. Acids Res.</i> 26:2536-2540, Oxford University Press (June 1998)				
	AS	11	Okano, M., et al., "Cloning and characterization of a family of novel mammalian DNA (cytosine-5) methyltransferases," <i>Nat. Genet.</i> 19:219-220, Nature Publishing Group (July 1998)				
	AT	11	Okano, M., et al., "DNA Methyltransferases Dnmt3a and Dnmt3b Are Essential for De Novo Methylation and Mammalian Development," <i>Cell</i> 99:247-257, Cell Press (October 1999)				
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	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	12	Okano, M., and Li, E., "Genetic Analyses of DNA Methyltransferase Genes in Mouse Model System," <i>J. Nutr.</i> 132:2462S-2465S, American Institute of Nutrition (August 2002)				
	AS	12	Pradhan, S., <i>et al.</i> , "Baculovirus-mediated expression and characterization of the full-length murine DNA methyltransferase," <i>Nucl. Acids Res.</i> 25:4666-4673, Oxford University Press (November 1997)				
	AT	12	Qu, G.-Z., <i>et al.</i> , "Satellite DNA hypomethylation vs. overall genomic hypomethylation in ovarian epithelial tumors of different malignant potential," <i>Mutat. Res.</i> 423:91-101, Elsevier Science (January 1999)				
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	13	Razin, A., and Cedar, H., "DNA methylation and embryogenesis," in <i>DNA Methylation: Molecular Biology and Biological Significance</i> , Jost, J.P., and Saluz, H.P., eds., Birkhäuser Verlag, Basel, Switzerland, pp. 343-357 (1993)				
	AS	13	Reid, G.K., <i>et al.</i> , "Selective inhibition of DNA methyltransferase enzymes as a novel strategy for cancer treatment," <i>Curr. Opin. Mol. Ther.</i> 4:130-137, Current Drugs (April 2002)				
	AT	13	Robertson, K.D., <i>et al.</i> , "The human DNA methyltransferases (DNMTs) 1, 3a and 3b: coordinate mRNA expression in normal tissues and overexpression in tumors," <i>Nucl. Acids Res.</i> 27:2291-2298, Oxford University Press (June 1999)				
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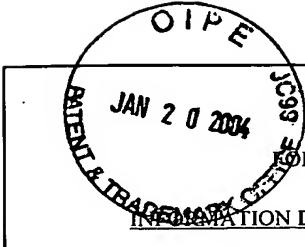
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	14	Stöger, R., <i>et al.</i> , "Maternal-Specific Methylation of the Imprinted Mouse <i>Igf2r</i> Locus Identifies the Expressed Locus as Carrying the Imprinting Signal," <i>Cell</i> 73:61-71, Cell Press (1993)				
	AS	14	Szyf, M., <i>et al.</i> , "Induction of Myogenic Differentiation by an Expression Vector Encoding the DNA Methyltransferase cDNA Sequence in the Antisense Orientation," <i>J. Biol. Chem.</i> 267:12831-12836, The American Society for Biochemistry and Molecular Biology, Inc. (1992)				
	AT	14	Szyf, M., and Detich, N., "Regulation of the DNA Methylation Machinery and Its Role in Cellular Transformation," in <i>Progress in Nucleic Acid Research and Molecular Biology</i> , Moldave, K., ed., Academic Press, San Diego, CA, pp. 47-79 (August 2001)				
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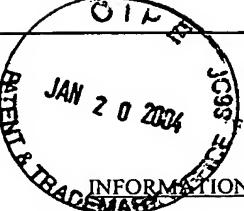
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	15	Trasler, J.M., <i>et al.</i> , "DNA Methyltransferase in Normal and <i>Dnmt</i> ^{3a} / <i>Dnmt</i> ^{3b} Mouse Embryos," <i>Dev. Dyn.</i> 206:239-247, Wiley-Liss, Inc. (1996)				
	AS	15	Tremblay, K.D., <i>et al.</i> , "A paternal-specific methylation imprint marks the alleles of the mouse <i>H19</i> gene," <i>Nat. Genet.</i> 9:407-413, Nature Publishing Group (1995)				
	AT	15	Tucker, K.L., <i>et al.</i> , "Germ-line passage is required for establishment of methylation and expression patterns of imprinted but not of nonimprinted genes," <i>Genes & Develop.</i> 10:1008-1020, Cold Spring Harbor Laboratory Press (1996)				
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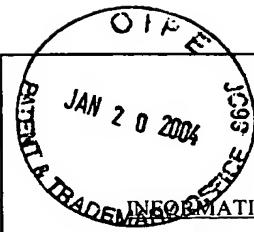


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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	<u>16</u>	Xie, S., <i>et al.</i> , "Cloning, expression and chromosome locations of the human DNMT3 gene family," <i>Gene</i> 236:87-95, Elsevier Science B.V. (August 1999)				
	AS	<u>16</u>	Yen, R.-W. C., <i>et al.</i> , "Isolation and Characterization of the cDNA encoding human DNA methyltransferase," <i>Nucl. Acids Res.</i> 20:2287-2291, Oxford University Press (1992)				
	AT	<u>16</u>	Yoder, J.A., and Bestor, T.H., "A candidate mammalian DNA methyltransferase related to pmt1p of fission yeast," <i>Hum. Mol. Genet.</i> 7:279-284, Oxford University Press (February 1998)				
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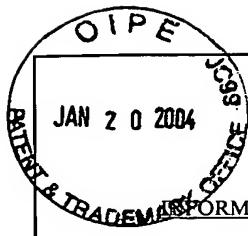
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	AR	17	Zuccotti, M., and Monk, M., "Methylation of the mouse <i>Xist</i> gene in sperm and eggs correlates with imprinted <i>Xist</i> expression and paternal X-inactivation," <i>Nat. Genet.</i> 9:316-320, Nature Publishing Group (1995)				
	AS	17	International Search Report for International Application No. PCT/US99/14373, mailed December 10, 1999, European Patent Office, Netherlands				
	AT	17	Dialog File 351, Accession No. 10305671, Derwent WPI English language abstract for WO 95/14772				
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	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	18	GenCore database. Sequence alignment between SEQ ID NO: 2 and Accession number AF067972 of Xie et al. Gene 236(1): 87-95, 1999, 3 sheets				
	AS	18	GenCore database. Sequence alignment between SEQ ID NO: 2 and Accession number AF068626 and AF068627 of Okano et al. Nat. Genet. 19(3): 219 and 220, 1998, 8 sheets				
	AT	18	GenCore nucleic acid and amino acid database. Sequence comparison between accession number AF067972 from Gene 1999 paper and Applicants' SEQ ID NO: 7 and 8, February 12, 2001				
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	AR	19	GenCore nucleic acid database. Sequence comparison between accession number AAT21884 from WO document 9514772-A1 and Applicants' SEQ ID NO: 1 and 3, June 1, 1995				
	AS	19	GenCore nucleic acid and amino acid database. Sequence comparison between sequence 47 of U.S. Patent 6,183,968 and Applicants' SEQ ID NO: 2 and 5-8, March 27, 1998				
	AT	19	GenCore nucleic acid and amino acid database. Sequence comparison between sequence accession number AF069625 from Nature Genetics 1998 paper and Applicants' SEQ ID NO: 5 and 6, December 6, 1999				
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